

## CLAIMS

What is claimed is:

1. A method for tissue augmentation or restoration in a mammal, said method comprising: injecting a polymer at a tissue site in need of augmentation and having a tissue temperature, said polymer comprising repeating peptide monomeric units selected from the group consisting of nonapeptide, pentapeptide and tetrapeptide monomeric units, wherein said monomeric units form a series of  $\beta$ -turns separated by dynamic bridging segments suspended between said  $\beta$ -turns, wherein said polymer has an inverse temperature transition  $T_i$  less than said tissue temperature, and wherein said polymer is injected as a water solution at coacervate concentration in the substantial absence of additional water.
2. The method of Claim 1 wherein said coacervate concentration has a viscosity at said tissue temperature of 1 to 100,000 millipoise.
3. The method of Claim 1 wherein said polymer is cross-linked but extrusible.
4. The method of Claim 1 wherein said polymer is a copolymer formed from one of said monomeric units and a second peptide unit containing 1-100 amino acids.
5. The method of Claim 4 wherein said second peptide unit contains 1-20 amino acids.
6. The method of Claim 1 wherein said polymer comprises a block or random copolymer comprising at least two of said monomeric units.
7. The method of Claim 1 wherein said polymer comprises an elastomeric polytetrapeptide or polypentapeptide.
8. The method of Claim 7 wherein said polymer comprises tetrapeptide units selected from the group consisting of VPGG (SEQ ID NO:16), GGVP (SEQ ID NO:41); GGFP (SEQ ID NO:42) and GGAP (SEQ ID NO:50).

9. The method of Claim 7 wherein said polymer comprises pentapeptide units selected from the group consisting of VPGVG (SEQ ID NO:17), GVGVP (SEQ ID NO:20), GKGVP (SEQ ID NO:43), GVGFP (SEQ ID NO:44), GFGFP (SEQ ID NO:45), GEGVP (SEQ ID NO:48), GFGVP (SEQ ID NO:49) and (GVGIP) (SEQ ID NO:51).

10. The method of Claim 1 wherein said polymer is a copolymer comprised of tetrapeptide and pentapeptide units.

11. The method of Claim 5 wherein said second peptide unit comprises the cell attachment sequence, GRGDSP (SEQ ID NO:46).

12. The method of Claim 5 wherein said second peptide unit comprises GVGVP (SEQ ID NO:47) or VGVAPG (SEQ ID NO:52).

13. The method of Claim 4 wherein said second peptide unit comprises a cell attachment sequence from the Type-III domains of fibronectin, vitronectin, tenascin, titan and other related cell attachment proteins.

14. The method of Claim 1 wherein said polymer comprises a plastic polypeptide.

15. The method of Claim 1 wherein said polymer is injected in combination with a further component selected from the group consisting of host-compatible cells and growth factors.

16. The method of Claim 1 further comprising injecting an osteogenic factor at said site.

17. The method of Claim 1 wherein said polymer is contained within a pharmaceutically acceptable liquid carrier, which further comprises one or more biologically active factors to aid in the healing or regrowth of natural tissue.

18. The method of Claim 17 wherein said factors are selected from the group consisting of heparin, epidermal growth factor, transforming growth factor- $\alpha$ , transforming growth factor- $\beta$ , platelet-derived growth factor, fibroblast growth factor, connective tissue activating peptides,  $\beta$ -thromboglobulin, insulin-like growth factors, tumor necrosis factors, interleukins, colony stimulating factors, erythropoietin, nerve growth factors, interferons, osteogenic factors and bone morphogenic proteins.

19. The method of Claim 1 wherein said tissue site is periurethral.

20. The method of Claim 1 wherein said tissue site is subdermal.

21. The method of Claim 1 wherein said tissue is soft tissue.

22. The method of Claim 1 wherein said tissue is hard tissue.

23. A method for tissue augmentation or restoration in a mammal, said method comprising the steps of

a) identifying a tissue site in need of tissue augmentation or restoration, said site having a site temperature ( $T_s$ ); and

b) injecting a polymer at the site, said polymer comprising repeating peptide monomeric units selected from the group consisting of pentapeptide and tetrapeptide monomeric units, alone or in combination, wherein said monomeric units form a series of  $\beta$ -turns separated by dynamic bridging segments suspended between said  $\beta$ -turns, and wherein (i) said polymer has an inverse temperature transition  $T_i$  less than  $T_s$ , (ii) said polymer is injected as a water solution at coacervate concentration in the substantial absence of additional water, and (iii) said coacervate has a viscosity at  $T_s$  of 1 to 100,000 millipoise.

24. The method of Claim 23 wherein said polymer is cross-linked but extrusible.

25. The method of Claim 23 wherein said polymer is a copolymer formed from one of said monomeric units and a second peptide unit containing 1-20 amino acids.
26. The method of Claim 23 wherein said polymer comprises a block or random copolymer comprising at least two different monomeric units.
27. The method of Claim 23 wherein said polymer comprises an elastomeric polytetrapeptide or polypentapeptide.
28. The method of Claim 27 wherein said polymer comprises tetrapeptide units selected from the group consisting of VPGG (SEQ ID NO:16), GGVP (SEQ ID NO:41); GGFP (SEQ ID NO:42) and GGAP (SEQ ID NO:50).
29. The method of Claim 27 wherein said polymer comprises pentapeptide units selected from the group consisting of VPGVG (SEQ ID NO:17), GVGVP (SEQ ID NO:20), GKGVP (SEQ ID NO:43), GVGFP (SEQ ID NO:44), GFGFP (SEQ ID NO:45), GEGVP (SEQ ID NO:48), GFGVP (SEQ ID NO:49) and (GVGIP) (SEQ ID NO:51).
30. The method of Claim 23 wherein said polymer is a copolymer comprised of tetrapeptide and pentapeptide units.
31. The method of Claim 25 wherein said second peptide unit is selected from the group consisting of GRGDSP (SEQ ID NO:46), GVGVP (SEQ ID NO:47) and VGVAPG (SEQ ID NO:52).
32. The method of Claim 23 wherein said polymer is injected in combination with a further component selected from the group consisting of host-compatible cells and growth factors.
33. The method of Claim 23 wherein said polymer is contained within a pharmaceutically acceptable liquid carrier, which further comprises one or more biologically active factors to aid in the healing or regrowth of natural tissue.

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34. The method of Claim 23 wherein said tissue site is periurethral, subdermal, tendon or cartridge.

35. A method for tissue restoration of intervertebral discs in a mammal, said method comprising: injecting a polymer into the depleted nucleus pulposus site, which has a site temperature, said polymer comprising repeating peptide monomeric units selected from the group consisting of nonapeptide, pentapeptide and tetrapeptide monomeric units, wherein said monomeric units form a series of  $\beta$ -turns separated by dynamic bridging segments suspended between said  $\beta$ -turns, wherein said polymer has an inverse temperature transition  $T_i$  less than said site temperature, and wherein said polymer is injected as a water solution at coacervate concentration in the substantial absence of additional water and swells to increase the pressure within said disc.

36. The method of Claim 35 wherein said coacervate has an elastic modulus at said site of  $5 \times 10^4$  to  $5 \times 10^6$  N/m<sup>2</sup>.

37. The method of Claim 35 wherein said polymer is cross-linked.

38. The method of Claim 35 wherein said polymer is a copolymer formed from one of said monomeric units and a second peptide unit containing 1-100 amino acids.

39. The method of Claim 38 wherein said second peptide unit contains 1-20 amino acids.

40. The method of Claim 35 wherein said polymer comprises a block or random copolymer comprising at least two of said monomeric units.

41. The method of Claim 35 wherein said polymer comprises an elastomeric polytetrapeptide or polypentapeptide.

42. The method of Claim 41 wherein said polymer comprises tetrapeptide units selected from the group consisting of VPGG (SEQ ID NO:16), GGVP (SEQ ID NO:41); GGFP (SEQ ID NO:42) and GGAP (SEQ ID NO:50).

43. The method of Claim 41 wherein said polymer comprises pentapeptide units selected from the group consisting of VPGVG (SEQ ID NO:17), GVGVP (SEQ ID NO:20), GKGVP (SEQ ID NO:43), GVGFP (SEQ ID NO:44), GFGFP (SEQ ID NO:45), GEGVP (SEQ ID NO:48), GFGVP (SEQ ID NO:49) and (GVGIP) (SEQ ID NO:51).

44. The method of Claim 35 wherein said polymer comprises at least one pentapeptide unit of (GVGIP) (SEQ ID NO:51).

45. The method of Claim 35 wherein at least one of said monomeric units contains an aromatic residue.

46. The method of Claim 45 wherein said aromatic residue is phenylalanine.

47. The method of Claim 35 wherein said polymer is a copolymer comprised of tetrapeptide and pentapeptide units.

48. The method of Claim 39 wherein said second peptide unit comprises the cell attachment sequence, GRGDSP (SEQ ID NO:46).

49. The method of Claim 39 wherein said second peptide unit comprises GVGVP (SEQ ID NO:47) or VGVAPG (SEQ ID NO:52).

50. The method of Claim 38 wherein said second peptide unit comprises a cell attachment sequence from the Type-III domains of fibronectin, vitronectin, tenascin, titan and other related cell attachment proteins.

51. The method of Claim 35 wherein said polymer comprises a plastic polypeptide.

52. The method of Claim 35 wherein said polymer is contained within a pharmaceutically acceptable liquid carrier, which further comprises one or more biologically active factors to aid in the healing or regrowth of natural tissue.

53. A method for tissue restoration of intervertebral discs in a mammal, said method comprising to step of injecting a polymer into the depleted nucleus pulposus site, which has a site temperature ( $T_s$ ), said polymer comprising repeating peptide monomeric units selected from the group consisting of pentapeptide and tetrapeptide monomeric units, alone or in combination, wherein said monomeric units form a series of  $\beta$ -turns separated by dynamic bridging segments suspended between said  $\beta$ -turns, and wherein (i) said polymer has an inverse temperature transition  $T_t$  less than  $T_s$ , (ii) said polymer is injected as a water solution at coacervate concentration in the substantial absence of additional water and swells to increase the pressure within said disc, and (iii) said coacervate has a shear modulus at  $T_s$  of  $5 \times 10^4$  to  $5 \times 10^6$  N/m<sup>2</sup>.

54. The method of Claim 53 wherein said polymer is cross-linked.

55. The method of Claim 53 wherein said polymer is a copolymer formed from said monomeric units and a second peptide unit containing 1-20 amino acids.

56. The method of Claim 53 wherein said polymer comprises a block or random copolymer comprising at least two different monomeric units.

57. The method of Claim 53 wherein said polymer comprises an elastomeric polytetrapeptide or polypentapeptide.

58. The method of Claim 57 wherein said polymer comprises tetrapeptide units selected from the group consisting of VPGG (SEQ ID NO:16), GGVP (SEQ ID NO:41); GGFP (SEQ ID NO:42) and GGAP (SEQ ID NO:50).

59. The method of Claim 57 wherein said polymer comprises pentapeptide units selected from the group consisting of VPGVG (SEQ ID NO:17), GVGVP (SEQ ID NO:20), GKGVP (SEQ ID NO:43), GVGFP (SEQ ID NO:44), GFGFP (SEQ ID NO:45), GEGVP (SEQ ID NO:48), GFGVP (SEQ ID NO:49) and (GVGIP) (SEQ ID NO:51).

60. The method of Claim 59 wherein said polymer comprises at least one pentapeptide unit of (GVGIP) (SEQ ID NO:51).

61. The method of Claim 53 wherein at least one of said monomeric units contains a phenylalanine residue.

62. The method of Claim 53 wherein said polymer is a copolymer comprised of tetrapeptide and pentapeptide units.

63. The method of Claim 55 wherein said second peptide unit is selected from the group consisting of GRGDSP (SEQ ID NO:46), GVGVP (SEQ ID NO:47) and VGVAPG (SEQ ID NO:52).

64. The method of Claim 53 wherein said polymer is contained within a pharmaceutically acceptable liquid carrier, which further comprises one or more biologically active factors to aid in the healing or regrowth of natural tissue.

65. A kit for tissue augmentation of a tissue, said tissue having a normal tissue temperature, comprising:

a syringe, a sterile wrapper surrounding said syringe and providing a sterile environment for said syringe, and a polymer contained in said syringe, wherein said polymer comprises repeating peptide monomeric units selected from the group consisting of nonapeptide, pentapeptide and tetrapeptide monomeric units, wherein said monomeric units form a series of  $\beta$ -turns separated by dynamic bridging segments suspended between said  $\beta$ -turns, and wherein said polymer has an inverse temperature transition  $T_i$  less than said tissue temperature.



66. The kit of Claim 65 wherein said polymer is present in said syringe as a water solution at coacervate concentration in the substantial absence of additional water.

67. The kit of Claim 65 wherein said polymer is contained within a pharmaceutically acceptable liquid carrier, which further comprises one or more biologically active factors to aid in the healing or regrowth of natural tissue.

68. The kit of Claim 67 wherein said factors are selected from the group consisting of heparin, epidermal growth factor, transforming growth factor- $\alpha$ , transforming growth factor- $\beta$ , platelet-derived growth factor, fibroblast growth factor, connective tissue activating peptides,  $\beta$ -thromboglobulin, insulin-like growth factors, tumor necrosis factors, interleukins, colony stimulating factors, erythropoietin, nerve growth factors, interferons, osteogenic factors and bone morphogenic proteins.

69. A kit for tissue restoration of intervertebral discs, said disc site having a normal tissue temperature, comprising:

a 13 to 19 gauge syringe, a sterile wrapper surrounding said syringe and providing a sterile environment for said syringe, and a polymer contained in said syringe, wherein said polymer comprises repeating peptide monomeric units selected from the group consisting of nonapeptide, pentapeptide and tetrapeptide monomeric units, wherein said monomeric units form a series of  $\beta$ -turns separated by dynamic bridging segments suspended between said  $\beta$ -turns, and wherein said polymer has an inverse temperature transition  $T_i$  less than said tissue temperature.

70. The kit of Claim 69 wherein said polymer is present in said syringe as a water solution at coacervate concentration in the substantial absence of additional water.

71. The kit of Claim 69 wherein said polymer is contained within a pharmaceutically acceptable liquid carrier, which further comprises one or more biologically active factors to aid in the healing or regrowth of natural tissue.

72. A protein based polymer for use in tissue augmentation or restoration comprising a polymer selected from the group consisting of the protein formulas of SEQ ID NOS: 9, 10, 12-15, 18, 21, 22, 25-27, 29, 34-40 and 53-61.

73. The protein based polymer of Claim 72 comprising a polymer selected from the group consisting of the protein formulas of SEQ ID NOS: 35, 36, 37, 38 and 39.

74. A protein based polymer for use in tissue restoration of intervertebral discs comprising a polymer selected from the group consisting of the protein formulas of SEQ ID NOS: 9, 10, 12-15, 18, 21, 22, 25-27, 29, 34-40 and 53-61.

75. The protein based polymer of Claim 74 comprising a polymer selected from the group consisting of the protein formulas of SEQ ID NOS: 54, 55, 56, 57, 58, 59 and 60.

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